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Of Title: Effects of Obesity Surgery on Overall and Disease-specific Mortality in a 5-Country, Population-based Study

Short Title: Obesity surgery and mortality

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Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; SMR, standardized mortality ratio.

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Abstract

Background & Aims: Bariatric surgery might reduce overall mortality from obesity. We investigated whether survival times of patients who have undergone bariatric surgery are similar to those of the general population levels and are longer than in obese individuals who did not receive surgery.

Methods: We performed a population-based cohort study of persons with a diagnosis of obesity listed in nationwide registries from Nordic countries, from 1980 through 2012. Bariatric surgery was analyzed in relation to all-cause mortality and the obesity-related morbidities cardiovascular disease, diabetes, cancer, and suicide. Poisson models provided standardized mortality ratios (SMRs) with 95% CIs. Multivariable Cox regression provided hazard ratios (HRs) for mortality in operated and non-operated participants.

Results: Among 505,258 participants, 49,977 underwent bariatric surgery. Overall all-cause SMR was increased after surgery (SMR=1.94; 95%CI 1.83-2.05) and increased with longer follow-up to 2.28 (95%CI 2.07-2.51) ≥15 years post-surgery. SMRs were increased for cardiovascular disease (SMR=2.39; 95%CI 2.17-2.63), diabetes (SMR=3.67; 95%CI 2.85-4.72), and suicide (SMR=2.39; 95%CI 1.96-2.92), but not for cancer (SMR=1.05; 95%CI 0.95-1.17), all with increasing SMRs over time. In non-operated obese participants, all-cause SMR was 2.15 (95%CI 2.11-2.20), which remained stable during follow-up. Compared to non-operated obese participants, bariatric surgery patients had decreased overall mortality from all causes (HR=0.63; 95%CI 0.60-0.66), cardiovascular disease (HR=0.57; 95%CI 0.52-0.63), and diabetes (HR=0.38; 95%CI 0.29-0.49), but increased mortality from suicide (HR=1.68; 95%CI 1.32-2.14). Cancer mortality was decreased overall (HR=0.84; 95%CI 0.76-0.93), but increased after ≥15 years of follow-up (HR=1.20; 95%CI 1.02-1.42).

Conclusion: In a study of persons with a diagnosis of obesity listed in nationwide registries of Nordic countries, we found that obese patients who undergo bariatric surgery have longer survival times than non-operated obese individuals, but their mortality is higher than that of the general population and increases with time. Obesity-related morbidities could account for these findings.

Keywords: Gastric bypass, metabolic syndrome, outcome, NordOSCO.

Introduction

The prevalence of obesity is high globally, with over 600 million obese adults (body mass index [BMI] $\geq$30 kg/m^2) in 2015, and is increasing.[1] Cardiovascular disease, diabetes, and cancer are common obesity-related morbidities, and also common causes of death.[1] Treatment of moderate obesity may include lifestyle intervention and medication, while obesity surgery is considered the most effective treatment of severe obesity (BMI $\geq$40 kg/m^2).[2] Compared to non-surgical weight loss treatment, obesity surgery can achieve a more pronounced and long-lasting weight reduction, resulting in less comorbidity and better overall survival at least during the initial years after surgery.[3-11] An exception is a reported increased risk of suicide following obesity surgery.[9, 12] Importantly, whether the survival after obesity surgery approaches to that of the general population and whether the survival remains better than that of non-operated individuals with obesity in the long term (>10 years) is uncertain. Thus, the present study aimed to test two main hypotheses: (1) The long-term survival of the severely obese individuals undergoing obesity surgery starts moving towards, but not equaling, that of the general population, and (2) obesity surgery results in a better long-term survival than in non-operated individuals with obesity. If evidence supporting these hypotheses are observed they might be due to reductions in mortality from obesity-related morbidities. The hypotheses were tested in a cohort study in all Nordic countries with long and complete follow-up.

Methods

Study design

This population-based cohort study followed a detailed pre-defined study protocol and examined how obesity surgery influences all-cause mortality and disease-specific mortality during the 33-year study period 1980 through 2012. The cohort, entitled the Nordic Obesity Surgery Cohort (NordOSCO), incorporated data from nationwide health data registers from all five Nordic countries, i.e. Denmark, Finland, Iceland, Norway, and Sweden, and has been described in a cohort profile publication.[13] The time required for all approvals and to collect, check, re-collect, and merge all data was 5½ years. The Nordic countries have similar and complete recording of hospital admissions and long and complete follow-up of death in all residents.[14] Reporting of patient admissions, diagnosis codes, and surgical procedures to the national health data registries is mandatory by law, and is linked to the remuneration of all Nordic hospitals.[14] Each Nordic resident is assigned a unique, personal identity code upon birth or immigration, which is used by governmental agencies, healthcare, and nationwide registries storing personal information for governmental and research purposes.[14] This personal identity code system enables accurate linkage of information between registries for each individual.[15, 16] The study was approved by all relevant ethical committees and data inspectorates in each of the participating countries.[13]

Obesity cohort

NordOSCo included all individuals with an obesity diagnosis recorded in any of the Nordic patient registries.[13] These registries hold nationwide information on in-hospital care and out-patient specialist care, including diagnoses and surgical procedures, with high concordance to the diagnoses and procedures recorded in the patient records.[17-19] The dates of recording of obesity diagnosis and obesity surgery in the registries varied between the countries, namely from 1996 to 2011 in Denmark, 1996 to 2012 in Finland, 1999 to 2012 in Iceland, 2007 to 2011 in Norway, and 1980 to 2012 in Sweden. Follow-up started on the first date of a recorded obesity diagnosis, but only within the study period in each country, and lasted until death, emigration (outside the Nordic countries), or the end of study period, whichever occurred first. Emigration dates were retrieved from complete national population registries.[13]

Exposure

The exposure was obesity surgery and participants with obesity who did not undergo obesity surgery were defined as unexposed. Obesity surgery included open or laparoscopic approach of any of the following five techniques: gastric bypass, vertical banded gastroplasty, gastric banding, other restrictive procedures, or blocking procedures, as determined by the specific surgical codes in the patient registries. Participants entered the study at the time of obesity diagnosis after the country-specific entry period. Participants contributed observations to the non-operated group from the date of obesity diagnosis until date of surgery, date of death, end of study period, or emigration, whichever came first. Participants contributed to the operated group from the date of obesity surgery until date of death, end of study period, or emigration. For participants who underwent obesity surgery, follow-up changed from the non-operated group (obesity diagnosis) to the operated group on the date of surgery. If the obesity diagnosis was recorded during the hospitalization of the obesity surgery, the follow-up started from the date of surgery. The registration of obesity surgery in the patient registries is 97% concordant with operation charts.[20]

Outcomes

The main outcome was all-cause mortality. Secondary outcomes were mortality specifically in the obesity-related morbidities cardiovascular disease, diabetes, cancer, and suicide. Dates and causes of death were obtained from the national death registries up until December 31, 2012. Death due to diabetes included deaths caused by any type of diabetes (although the vast majority was due to diabetes type 2). The completeness for all-cause mortality data in these registers is 100%, and at least 96% for causes of death.[21-23] In Finland, all death certificates are checked by forensic physicians, and completed with the physician or pathologist writing the death certificate when needed.[23] The data quality in the Norwegian cause of death registry has been rated in the best category in an external review.[22] In Sweden, the concordance between cause of death registry and the medical records data is very high, 98% in the age group <45 years and 91% for the age group 45-64 years.[21] The validity of deaths from suicide in the cause of death registries is high; a re-review of death certificates due to suspected suicide, unintentional and unclear deaths did not increase the overall number of suicides compared to registries in Denmark, Norway and Sweden.[24] In Finland, >90% of all persons who have died due to unclear reason, unintentional causes, or injury, and >99% of persons who died from suspected suicide undergo medico-legal or medical autopsy, after which the cause of death is recorded in the cause of death registry.[25]

Statistical analysis

First, the all-cause mortality in the obesity surgery cohort was compared with its corresponding background population and the non-operated obese cohort with its corresponding background population. The corresponding background population of each of these cohorts had the same distribution of age (5-year age group), sex, and country as the participants in the specific cohort. Standardized mortality ratios (SMRs) with 95% confidence intervals (CIs) were calculated. The SMRs were computed using a Poisson regression with outcome observed number of deaths in the study cohorts by age, sex, calendar year, and exposure status and offset variable expected deaths in the population by age, sex and calendar year. Confidence intervals were computed using a sandwich estimator of the variance. For the analyses, data were collapsed by age, sex, calendar year, and four categories of follow-up time to reduce bias of the standard error as data from the reference population was available as grouped data.

The expected numbers of death were derived from country-specific mortality rates categorized by sex, age (5-year categories), and calendar year (5-year categories), retrieved from the Nordic cause of death registries. Obesity surgery was treated as a time-dependent covariate. In stratified analyses, participants were grouped into follow-up periods after date of surgery or date of obesity diagnosis into 0-4 years, 5-9 years, 10-14 years, and ≥15 years. The five obesity surgery techniques were also analyzed separately.

Second, to estimate all-cause and disease-specific mortality comparing operated and non-operated participants with obesity, multivariable Cox regression with adjustment for potential confounders was used. The calculated hazard ratios (HR) with 95% CI were adjusted for age (continuous), sex (male or female), calendar year (continuous), country (Denmark, Finland, Iceland, Norway, or Sweden), and comorbidity (Charlson Comorbidity Index 0, 1, 2, or ≥3). Comorbidity was assessed using the most recent and well-validated Charlson Comorbidity Index,[26] which was based on diagnoses in the patient registries up to one year before the entry date into the cohort. This restriction in time was made to allow all relevant comorbidities to be included, but to avoid including comorbidities or complications due to obesity surgery. Sub-analyses were stratified by age groups (<30, 30-39, 40-49, or ≥50 years), sex (female or male), and follow-up periods (0-4 years, 5-9 years, 10-14 years, and ≥15 years). The proportionality assumption was verified using Schoenfeld residuals. There were no missing data.

All data management and statistical analyses were conducted by a senior biostatistician (G.S.), using Stata/MP version 15.1 (StataCorp LLC, College Station, TX, USA).

Results

Patients (Table 1)

Of all 505,258 cohort participants with obesity, 49,977 (9.9%) underwent obesity surgery (312,128 person-years of follow-up) and 494,842 did not (3,188,969 person-years, including years prior to any obesity surgery). In the obesity surgery group, the median age was lower and the frequency of women was higher than in the non-operated group. Sweden contributed most participants in the obesity surgery group (72.1%) and Denmark contributed most participants in the non-operated group (41.3%). In the surgery group, the most common obesity surgical technique was gastric bypass (73.4%).

Mortality in operated individuals with obesity compared to population levels (Table 2)

The overall (entire study period) SMR of all-cause mortality after obesity surgery was 1.94 (95% CI 1.83-2.05). The SMRs of all-cause mortality increased with follow-up periods from 1.62 (95% CI 1.48-1.79) 0-4 years after surgery to 2.28 (95% CI 2.07-2.51) ≥15 years after surgery (Figure 1). Different obesity surgical techniques yielded similar SMRs (Supplementary Table 1). For cardiovascular disease, the overall SMR was 2.39 (95% CI 2.17-2.63) and the SMR increased from 1.84 (95% CI 1.54-2.20) 0-4 years after surgery to 2.71 (95% CI 2.30-3.18) ≥15 years after surgery. For diabetes, the overall SMR was 3.67 (95% CI 2.85-4.72), with increasing SMRs from 1.26 (95% CI 0.60-2.64) 0-4 years after surgery to 6.26 (95% CI 4.54-8.64) ≥15 years after surgery. For cancer, the overall SMR was not increased (SMR 1.05, 95% CI 0.95-1.17), but an increase was observed ≥15 years after surgery (1.46, 95% CI 1.28-1.67). For suicide, the overall SMR was 2.39 (95% CI 1.96-2.92), and the SMR increased from 1.93 (95% CI 1.43-2.61) 0-4 years after surgery to 3.39 (2.11-5.44) ≥15 years after surgery.

Mortality in non-operated individuals with obesity compared to population levels (Table 2)

In obese participants who did not undergo obesity surgery, the overall all-cause SMR was 2.15 (95% CI 2.11-2.20), with SMRs remaining stable during follow-up (Figure 1). The disease-specific overall SMRs were 2.26 (95% CI 2.15-2.37) for cardiovascular disease, 6.89 (95% CI 6.54-7.27) for diabetes, 1.25 (95% CI 1.23-1.28) for cancer, and 1.15 (95% CI 1.06-1.26) for suicide, all with stable SMRs during follow-up.

Mortality in operated compared to non-operated participants with obesity (Table 3)

Participants who had undergone obesity surgery had a lower HRs of overall all-cause mortality compared to non-operated participants with obesity (adjusted HR 0.63, 95% CI 0.60-0.66). The HRs remained decreased for all follow-up periods after surgery, and the HR was 0.74 (95% CI 0.68-0.81) after ≥15 years of follow-up. The HRs decreased with age from 1.03 (95% CI 0.83-1.27) among participants younger than 30 years to 0.54 (95% CI 0.50-0.58) in individuals ≥50 years. The HRs were similar between the sexes as well as for the different obesity surgical techniques (Supplementary Table 2). Compared to the non-operated group, the operated group had decreased HRs of overall mortality from cardiovascular disease (HR 0.57, 95% CI 0.52-0.63) and diabetes (HR 0.38, 95% CI 0.29-0.49), and the HRs remained decreased over follow-up periods (Table 3). For cancer, the overall mortality was decreased (HR 0.84, 95% CI 0.76-0.93), but the HRs increased over follow-up periods, and the HR was increased after ≥15 years of follow-up (HR 1.20, 95% CI 1.02-1.42). The overall HR of mortality from suicide was increased (HR 1.68, 95% CI 1.32-2.14), and this increase remained over follow-up periods. For all mortality outcomes, the point estimates were higher in the latest (≥15 years) compared to the initial (0-4 years) follow-up period.

Discussion

This study indicates that individuals who undergo obesity surgery remain at a higher all-cause mortality compared to the background population, with increasing SMRs over time after surgery. The overall SMRs were increased for cardiovascular disease, diabetes, and suicide, but not for cancer, and all disease-specific SMRs increased with longer follow-up after surgery. Compared to non-operated participants with obesity, the operated patients had overall decreased mortality from all causes, cardiovascular disease, diabetes, and cancer (except for increased cancer mortality in the ≥15 years follow-up period), whereas mortality due to suicide was increased, and the HRs for all outcomes were higher in the last follow-up period compared to the first.

Strengths of the study include the population-based design, availability of a corresponding background population for comparison, large sample size, and the long and complete follow-up. The high quality of the registry data in the Nordic countries has been verified in multiple studies, but some limited non-differential misclassification might still exist. This might make the observed associations appear smaller than they are. The Nordic populations share sociodemographic characteristics, genetic background, cultural traditions, and norms, and have similar and publicly funded healthcare-, social- and registration systems, as well as mortality rates. Furthermore, the guidelines for BMI and comorbidity requirements for bariatric surgery are similar in these countries.[27, 28] Therefore, combining data from these countries does not introduce much heterogeneity, but improves statistical power and facilitates generalisability.[14] Patients selected for obesity surgery may be healthier than non-operated patients with obesity and in short follow-up even less likely to die than the background population. Yet, their severe obesity and associated comorbidities together with a risk of postoperative mortality act against such selection bias. A limitation is the lack of data on some potential confounders not adjusted for, mainly BMI, socioeconomic status, tobacco smoking, and alcohol use. However, weight change lies in the proposed causal pathway between obesity surgery and survival and is therefore not a confounder. Moreover, individuals selected for obesity surgery constitute a relatively homogenous group regarding BMI and comorbidity.[27] The lack of BMI in the non-operated patients with obesity could be seen as a major limitation, but this only affects the comparison between the operated and non-operated patients with obesity, not the analysis of SMRs. Moreover, the results on the comparisons between operated and non-operated individuals with obesity are in line with previous studies on the topic.[8-10] One might argue that the lack of adjustment for socioeconomic status might affect the access to surgery. However, in all the Nordic countries, healthcare, including bariatric procedures, are covered by the national social insurance, and therefore socioeconomic status is not associated to access to treatment (i.e. the exposure) and should not be a confounder. Smoking and alcohol use are indirectly reflected in the Charlson comorbidity score. As the risk of chronic obstructive pulmonary disease (COPD) is linearly associated with smoked pack-years and cigarettes per day,[29] and the prevalence of smokers is much higher in a population with COPD compared to those not having COPD,[30] the adjustment for comorbidity is likely to catch the most heavy smokers. Similarly, alcohol consumption is strongly associated with liver disease,[31] and the adjustment for comorbidity therefore reduces the confounding by heavy alcohol use. These were adjusted for in the Cox regression analysis without changing the risk estimates, indicating no or limited confounding by these factors. Because the reporting of surgical procedures to the national patient registries is mandatory and the hospital reimbursement depends on this reporting, the assessment of obesity surgery should be complete. A limitation, however, is that obesity diagnosis in non-operated participants with obesity is likely under-reported in the registries, and those who are diagnosed might be a selected group of older patients with more comorbidities. However, the adjustment for age, comorbidity and other potential confounders in the Cox regression analyses should counteract biased risk estimates. The lack of adjustment for psychiatric conditions can be seen as a limitation regarding the analysis of suicide. However, psychiatric conditions are more likely to be in the causal pathway leading to suicide rather than confound the association, and should therefore not be adjusted for. Also, there is no validated psychiatric comorbidity scale that can be used in the analyses.

It has been unclear whether the survival after obesity surgery approaches that of the corresponding background population. A Swedish study comparing 13,273 individuals who had undergone obesity surgery (some of whom are also included in the present study) with age- and sex-matched population controls suggested a slightly increased all-cause mortality after obesity surgery,[32] but changes over time after surgery and cause-specific mortality were not assessed. A population-based cohort study from the United States found increased age- and sex-specific mortality rates in obesity surgery patients (n=16,683) compared to the general population, and cardiovascular death specifically,[12] but the follow-up was limited (only 20% were followed up for 5 years), and other disease-specific causes of death were not examined. The present study, with a much larger sample size and longer follow-up than previous studies, shows increased mortality after obesity surgery compared to the background population, and interestingly, the mortality increased over time compared to the population levels. A possible explanation for the overall increased mortality rates is that obesity surgery rarely leads to normalized weight, but the average weight remains higher than that of the population.[33, 34] This is supported by the relatively stable SMRs in the non-operated group over time, who are likely to have stable or slowly increasing body weight. A Swedish study showed that patients undergoing obesity surgery had lost a mean of over 30kg of their weight at 1 year of follow-up, and that the weight remained 20kg lower compared to the baseline in the long-term.[34] A possible reason for the increasing mortality rates over time after surgery is weight gain; up to 50% of obesity surgery patients regain weight within two years of surgery,[35] and new comorbidities that increase the risk of cardiovascular and diabetic deaths may develop over time.[33] However, those that manage to lose weight and maintain the weight loss seem to have a long-lasting resolution of comorbidity.[33] In a study from the United States, achieving BMI under 30 one year postoperatively was associated to resolution of comorbidities.[36] Compared to the background population, excess mortality among the obesity surgery group was found specifically in cardiovascular disease, diabetes, and suicide. However, the cancer mortality returned to that of the population level for up to 15 years after obesity surgery, after which it was increased. This late increase in cancer mortality might be due to the longer latency interval between weight change and cancer development compared to cardiovascular diseases and diabetes. However, this increase in cancer mortality might be due to lower mortality from competing causes, such as lower cardiovascular mortality in the obesity surgery group. As more than 5000 patients representing three main types of surgery, namely gastric bypass, gastric banding and vertical banded gastroplasty, were included, the study should be generalizable to all patients undergoing these types of surgeries. Furthermore, the risk of mortality after different types of surgery were similar, with the exception of having a slightly higher risk after blocking procedures. As there are major differences in weight loss outcomes between these surgery types according to a meta-analysis,[37] the similar mortality rates between the surgery types in this study do not support the hypothesis that weight loss alone mediates mortality outcomes after obesity surgery. Taken together, the mortality of the patients undergoing obesity surgery does not approach that of the country-, age- and sex-adjusted general population, but the differences instead increase over time.

In line with the present study, previous larger studies comparing mortality in obesity surgery patients with non-operated patients with obesity have shown decreased all-cause mortality following obesity surgery, but these earlier studies have had shorter follow-up.[8-11] Interestingly, the current study found that the reduction in mortality remained over time, although the HRs were higher with longer follow-up periods. A decreasing mortality was found with increasing age, and no survival advantage was found in patients <30 years at obesity surgery; an observation supported by a study from the United States comparing 7,925 patients undergoing obesity surgery with an equal number of matched controls with obesity.[38] Obesity-related morbidities might take time to develop, and therefore the influence of obesity surgery might not be seen in younger patients.[39] Compared to non-operated participants with obesity of the present study, the obesity surgery patients had decreased mortality from obesity-related diseases, i.e. cardiovascular diseases, diabetes, and cancer, except for the increased risk of cancer mortality seen after ≥15 years of follow-up. Reductions in the occurrence of diabetes[40] and cardiovascular events, [41] after obesity surgery have been identified in earlier studies. A study indicated that recovery from diabetes following obesity surgery may be reduced from 72% at 2 years, to 30% at 10 years after surgery.[34] At 10 years after obesity surgery, newly diagnosed diabetes (7%), hypertension (41%), and hypertriglyceridemia (17%) often occur in patients without these comorbidities before surgery.[42] Taken together, the present study confirms the findings of previous studies that obesity surgery decreases mortality compared to controls with obesity, and additionally suggests that this decrease is long-lasting, also after 15 years of follow-up.

The mortality from suicide was substantially increased after obesity surgery compared to both the background population and non-operated participants with obesity, and the risk estimates tended to increase over time after surgery. Suggested mechanisms behind this phenomenon include changes that might occur after obesity surgery, i.e. unexpected recurrence of medical comorbidities,[43] surgical complications,[44] impulsiveness related to increased sensitivity to alcohol,[45, 46] decreased absorption of medications such as antidepressants,[47] psychosocial factors including persistent depression symptoms,[48] and decreased emotional well-being related to unforeseen weight gain.[43] A previous study in Sweden found that suicide risk was increased in bariatric surgery patients, even after adjustment for previous psychiatric care and medication use, and that those that committed suicide had similar or even greater weight loss than those who did not commit suicide.[49] The increased suicide rates after obesity surgery seen in the present study are in line with some previous studies,[12, 38] but an important finding of this study is that the suicide rate increased over time to more than 3-fold that of the general population after ≥15 years of surgery.

In conclusion, this all-Nordic population-based cohort study indicates that obesity surgery patients have lower mortality rates than non-operated patients with obesity, but higher mortality than the corresponding background population, a difference that increases over time after surgery. These findings may at least partly be explained by mortality from cardiovascular disease, diabetes, cancer, and suicide.

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Figure legends

Figure 1. The standardized mortality ratios (SMR) over time for obese patients undergoing surgery and not undergoing surgery.

Table 1. Characteristics of all 505,258 participants with obesity in a Nordic cohort

	No obesity surgery n=494,842 Number (%)	Obesity surgery n=49,977 Number (%)
Person-years of follow-up	3,188,969 (100.0)	312,128 (100.0)
Age at entry, years		
<30	98,249 (19.8)	7,815 (15.6)
30-39	95,887 (19.4)	14,388 (28.8)
40-49	84,560 (17.1)	15,922 (31.9)
≥50	216,146 (43.7)	11,852 (23.7)
Sex		
Male	160,435 (32.4)	12,730 (25.5)
Female	334,407 (67.6)	37,247 (74.5)
Country		
Denmark	204,263 (41.3)	3,269 (6.5)
Finland	87,450 (17.7)	4,429 (8.9)
Iceland	15,213 (3.1)	731 (1.5)
Norway	33,866 (6.8)	5,507 (11.0)
Sweden	154,050 (31.1)	36,041 (72.1)
Calendar year at entry		
<1990	21,004 (4.2)	2,334 (4.7)
1990-1999	85,280 (17.2)	6,751 (13.5)
2000-2004	76,611 (15.5)	3,172 (6.4)
2005-2009	190,763 (38.6)	15,553 (31.1)
≥2010	121,184 (24.5)	22,167 (44.4)
Follow-up time, years		
≤4	259,929 (52.5)	24,563 (49.1)
5-9	133,544 (27.0)	10,818 (21.6)
≥10	101,369 (20.5)	14,596 (29.2)
Charlson Comorbidity Index		
0	415,494 (84.0)	46,648 (93.3)
1	71,119 (14.4)	3,122 (6.3)
2	7,234 (1.5)	191 (0.4)
≥3	995 (0.2)	16 (0.0)
Obesity surgical technique		
Gastric bypass	Not applicable	36,678 (73.4)
Vertical banded gastroplasty	Not applicable	5,487 (11.0)
Gastric banding	Not applicable	5,450 (10.9)
Other restrictive procedures	Not applicable	1,578 (3.2)
Blocking procedures	Not applicable	784 (1.5)
Causes of mortality		
All-cause	75,345 (15.2)	1,784 (3.6)
Cardiovascular diseases	30,740 (6.2)	525 (1.1)
Diabetes	5,100 (1.0)	64 (0.1)
Cancer	13,880 (2.8)	422 (0.8)
Suicide	561 (0.1)	98 (0.2)

Table 2. Standardized mortality ratios (SMRs) and 95% confidence intervals (CI) in participants with obesity who have undergone obesity surgery and not, compared with the background population

	Non-operated with obesity		Obesity surgery	
Cause of death stratified by follow-up period	**Observed / Expected* number of deaths**	**SMR (95% CI)**	**Observed / Expected* number of deaths**	**SMR (95% CI)**
All causes				
Total	75,345 / 34,982	2.15 (2.11-2.20)	1,784 / 922	1.94 (1.83-2.05)
0-4 years	35,021 / 16,204	2.16 (2.09-2.24)	508 / 313	1.62 (1.48-1.79)
5-9 years	20,244 / 9,673	2.09 (2.01-2.18)	348 / 174	2.00 (1.75-2.29)
10-14 years	12,052 / 5,500	2.19 (2.07-2.32)	328 / 172	1.91 (1.66-2.20)
≥15 years	8,028 / 3,605	2.23 (2.10-2.36)	600 / 263	2.28 (2.07-2.51)
Cardiovascular				
Total	30,740 / 13,613	2.26 (2.15-2.37)	525 / 220	2.39 (2.17-2.63)
0-4 years	14,249 / 6,175	2.31 (2.15-2.48)	118 / 64	1.84 (1.54-2.20)
5-9 years	8,377 / 3,778	2.22 (2.03-2.42)	108 / 41	2.66 (2.17-3.26)
10-14 years	4,926 / 2,155	2.29 (2.03-2.58)	105 / 43	2.43 (1.90-3.09)
≥15 years	3,188 / 1,504	2.12 (1.85-2.42)	194 / 72	2.71 (2.30-3.18)
Diabetes				
Total	5,100 / 740	6.89 (6.54-7.27)	64 / 18	3.67 (2.85-4.72)
0-4 years	2,067 / 335	6.17 (5.65-6.73)	7 / 6	1.26 (0.60-2.64)
5-9 years	1,455 / 212	6.87 (6.27-7.53)	13 / 3	4.09 (2.46-6.79)
10-14 years	952 / 116	8.21 (7.25-9.30)	10 / 3	3.04 (1.78-5.17)
≥15 years	626 / 77	8.14 (6.91-9.60)	34 / 5	6.26 (4.54-8.64)
Cancer				
Total	13,880 / 11,067	1.25 (1.23-1.28)	422 / 401	1.05 (0.95-1.17)
0-4 years	6,876 / 5,259	1.31 (1.27-1.35)	82 / 132	0.62 (0.50-0.77)
5-9 years	3,673 / 3,052	1.20 (1.15-1.26)	81 / 77	1.05 (0.85-1.31)
10-14 years	2,089 / 1,708	1.22 (1.16-1.29)	92 / 77	1.19 (0.95-1.48)
≥15 years	1,242 / 1,049	1.18 (1.08-1.29)	167 / 114	1.46 (1.28-1.67)
Suicide				
Total	561 / 486	1.15 (1.06-1.26)	98 / 41	2.39 (1.96-2.92)
0-4 years	344 / 274	1.26 (1.13-1.40)	41 / 21	1.93 (1.43-2.61)
5-9 years	121 / 125	0.96 (0.81-1.16)	22 / 9	2.56 (1.69-3.87)
10-14 years	59 / 57	1.03 (0.77-1.38)	17 / 6	2.92 (1.74-4.91)
≥15 years	37 / 30	1.24 (0.91-1.70)	19 / 5	3.39 (2.11-5.44)

*Sex-, age-, calendar year- and country-specific mortality rate rounded to nearest integer.

Table 3. Hazard ratios (HRs) and 95% confidence intervals (CIs) of mortality comparing participants with obesity who have undergone obesity surgery with non-operated participants with obesity

		No obesity surgery	Obesity surgery	
Cause of death		**Number of deaths / person-years***	**Number of deaths / person-years**	**HR (95% CI)†***
All causes				
Follow-up	Total	75,345 / 3,188,969	1,784 / 312,128	0.63 (0.60-0.66)
	0-4 years	35,021 / 1,821,156	508 / 163,387	0.60 (0.54-0.66)
	5-9 years	20,244 / 793,408	348 / 64,232	0.67 (0.59-0.75)
	10-14 years	12,052 / 363,009	328 / 43,372	0.65 (0.58-0.73)
	≥15 years	8,028 / 211,396	600 / 41,136	0.74 (0.68-0.81)
Age	<30 years	921 / 613,667	132 / 60,943	1.03 (0.83-1.27)
	30-39 years	2,298 / 602,666	334 / 96,251	0.85 (0.74-0.97)
	40-49 years	6,401 / 584,928	601 / 94,852	0.65 (0.60-0.72)
	≥50 years	65,725 / 1,387,698	717 / 60,082	0.54 (0.50-0.58)
Sex	Male	31,120 / 1,021,086	656 / 71,429	0.65 (0.60-0.71)
	Female	44,225 / 2,167,883	1,128 / 240,699	0.62 (0.58-0.66)
Cardiovascular				
Follow-up	Total	30,740 / 3,188,969	525 / 312,128	0.57 (0.52-0.63)
	0-4 years	14,249 / 1,821,156	118 / 163,387	0.43 (0.35-0.51)
	5-9 years	8,377 / 793,408	108 / 64,232	0.58 (0.48-0.70)
	10-14 years	4,926 / 363,009	105 / 43,372	0.55 (0.45-0.67)
	≥15 years	3,188 / 211,396	194 / 41,136	0.74 (0.64-0.85)
Diabetes				
Follow-up	Total	5,100 / 3,188,969	64 / 312,128	0.38 (0.29-0.49)
	0-4 years	2,067 / 1,821,156	7 / 163,387	0.20 (0.10-0.42)
	5-9 years	1,455 / 793,408	13 / 64,232	0.42 (0.24-0.72)
	10-14 years	952 / 363,009	10 / 43,372	0.26 (0.14-0.48)
	≥15 years	626 / 211,396	34 / 41,136	0.53 (0.38-0.75)
Cancer				
Follow-up	Total	13,880 / 3,188,969	422 / 312,128	0.84 (0.76-0.93)
	0-4 years	6,876 / 1,821,156	82 / 163,387	0.47 (0.38-0.59)
	5-9 years	3,673 / 793,408	81 / 64,232	0.86 (0.69-1.08)
	10-14 years	2,089 / 363,009	92 / 43,372	0.94 (0.76-1.16)
	≥15 years	1,242 / 211,396	167 / 41,136	1.20 (1.02-1.42)
Suicide				
Follow-up	Total	561 / 3,188,969	98 / 312,128	1.68 (1.32-2.14)
	0-4 years	344 / 1,821,156	41 / 163,387	1.26 (0.89-1.77)
	5-9 years	121 / 793,408	22/ 64,232	2.19 (1.36-3.52)
	10-14 years	59 / 363,009	17 / 43,372	2.38 (1.36-4.18)
	≥15 years	37 / 211,396	18 / 41,136	2.14 (1.20-3.82)

* Sex-, age-, calendar year- and country-specific mortality rate rounded to nearest integer.
†Adjusted for age, sex, calendar year, country and comorbidity (excluding the variable analyzed)